

Application No.: 09/701,586

Inventor: Kock et al.

Reply to Notice of Non-Complaint Amendment of 25 September 2006

Docket No.: 49100

REMARKS/ARGUMENTS

Claims 1-3 and 33-60 are currently pending. Claims 1-3 are amended. Claims 33-60 are new. Support for the new claims can be found on pages 5 and 6 of the instant Specification. Claim 2 has been amended and the sequences listed in this claim have been put into separate dependent claims 2 and 33. Similarly, the sequences of claim 3 have been put in separate dependent claims 3, 34-37. New claim 38 has support in the instant Specification on page 5, lines 1-13. Claims dependent therefrom find support in claims 2 and 3, and in the instant specification on page 5, lines 15-34. New claim 47 finds support in claim 1 and the instant Specification on page 4, lines 29-40. Claims dependent therefrom find support in the instant Specification throughout page 5. No new material has been added.

Rejection under 35 USC §112 ¶1

Claims 1-3 stand rejected as allegedly non-enabled. Applicants respectfully disagree.

Regarding the enablement requirement of §112, the Federal Circuit has held that “[t]he specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without ‘undue experimentation’” (*Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1334 (Fed. Cir. (2003))). The claims are fully enabled by the Specification of the instant application in combination with the general knowledge of one of ordinary skill in the art.

Applicants have provided specific guidance for the modification of PARPs. The Examiner is directed to the instant specification, starting at line 39 of page 18, wherein the Applicants disclose the selection process for exchanges of amino acids. Applicants disclose the ability "to replace certain amino acids with those of similar physiochemical properties (bulk, basicity, hydrophobicity, etc.)" and provide examples of such substitutions, e.g. arginine for lysine. (See, page 19, lines 10-15). Further, Applicants disclose that it is also possible for more than one amino acid to be substituted, added or deleted or that a combination of these may be employed. Further still, Applicants respectfully assert that the recitation in claim 1 of a

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functional equivalent thereof which is at least 85% homologous is well supported as this percentage within the range of disclosed comparable identities for human PARP1, PARP2 and PARP3 - all of which are functional.

The Examiner asserts that modification of the specific amino acid positions within a given protein sequence is unpredictable and that one of skill in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification. Applicants respectfully disagree. The Examiner is directed to MPEP 2164.04 which states in regards to an enablement rejection, quoting *In re Marzocchi*, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement" (439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)(emphasis in original)). The Examiner has provided no evidence to support the above statement that the skilled artisan would expect **any** tolerance to diminish. If, contrary to Applicants' assertions that the instant invention is enabled, the Examiner has used information from examples not of record, Applicants respectfully request an Examiner's affidavit indicating the use of personal knowledge and allowance for Applicants to respond to said personal knowledge.

Additionally, the Examiner makes assertions regarding substituting amino acids, the predictability of results and obtaining the desired activity in the end product. Applicants respectfully assert that one of ordinary skill in the art would be able to determine to a sufficient degree, as to not require undue experimentation, amino acid substitutions. First, a skilled artisan would know that in certain positions, certain amino acid changes would render the subsequent protein inactive and would avoid using said substitutions. Along those lines, MPEP 2164.08(b) clearly states that "[t]he presence of inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled." Thus, Applicants respectfully assert that even if the skilled artisan substituted an amino acid at a non-optimum position, said invention is still enabled. Second, computational techniques were available at the time of filing for protein structural predictions based on sequence listings. The Examiner is directed to, for example, the

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Boston University Protein Sequence Analysis server (available at <http://bmerc-www.bu.edu/psa/>), which has been available since at least the filing date of this application. Consequently, modification of the instant claimed sequence in regards to the instant claims, would have been sufficiently routine to one of ordinary skill in the art.

Further, the Examiner asserts that "it is not routine in the art to screen for multiple substitutions or multiple modifications" (11 January 2006 Office Action, page 4). Applicants respectfully assert that the Examiner need only look to the USPTO itself for references for the screening that allegedly is "not routine." The numerous Affymetrix patents clearly show that large scale screening was and is state of the art and that a comparison of a sufficient number of sequences of PARPs to the disclosed PARPs **can** be performed; no undue experimentation would be required.

In this regard, The Examiner has provided no evidence to support the assertions of undue experimentation. The Examiner, in the 11 January 2006 Office Action states at least the following:

1. "Because of this lack of guidance, the extended experimentation that would be required ..." Page 5
2. "It would require undue experimentation for one skilled in the art to arrive as the majority of those polypeptides of the claimed genus." Page 5
3. "[T]he experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue." Pages 5-6

Applicants respectfully disagree. In order to establish a *prima facie* rejection, the Examiner must provide evidence of the necessity of said "undue experimentation." Along these lines, the Examiner has not stated why one skilled in the art could not supply the allegedly needed enabling information without undue experimentation. If the Examiner has personal knowledge regarding experimentation volume, Applicants respectfully request submission of an Examiner's affidavit and thereafter be provided a full and fair opportunity to respond. In the absence of such evidence or an affidavit, Applicants respectfully request that this rejection be withdrawn.

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In sum, Applicants respectfully assert that the instant claims are enabled based upon the requirements of §112, the MPEP and the rulings handed down from the Federal Circuit. One of ordinary skill in the art would have been able to practice the instant invention without undue experimentation based on a combination of the contents of the instant Specification when analyzed by the skill in the art at the time of filing. Accordingly, Applicants respectfully request withdrawal of the instant enablement rejection and favorable action is solicited.

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Conclusion

Applicants respectfully submit that the present application is in condition for allowance, which action is courteously requested. Please charge any shortage in fees due in connection with the filing of this paper to Deposit Account 14.1437. Please credit any excess fees to such account.

Respectfully submitted,
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